1654

Attorney Docket No. 9233-63

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Ekwuribe et al.
Serial No.: 09/873,797
Filed: June 4, 2001
For: Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same

Confirmation No.: 2859
Group Art Unit: 1654

December 23, 2003

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Sir:

Attached is a list of documents on Form PTO-1449, along with a copy of each listed document. It is requested that these documents be considered by the Examiner and officially made of record in accordance with the provisions of 37 C.F.R. § 1.97 and Section 609 of the MPEP.

Also attached is a Declaration of James Gordon Still under 37 C.F.R. § 1.132 in which Dr. Still provides information about the slides that are included on the attached PTO Form 1449 as items 93 and 98. Although applicants provide these slides to the examiner in the interest of full disclosure in accordance with applicant's duty, it is applicants' belief that these slides are not "printed publications" as set forth in 35 U.S.C. § 102(b) and are thus not prior art to the claimed invention. Applicants base this belief on a comparison of the facts in this case as set forth in Dr. Still's Declaration with the facts set forth in *Regents of the University of California v. Howmedica, Inc.* [210 U.S.P.Q. 727 (D.N.J. 1981); *aff'd,* 676 F.2d 687 (3rd Cir. 1982); copy enclosed], in which the court determined that slides shown during an oral presentation did not constitute a "printed publication" within the meaning of 35 U.S.C. § 102(b). Because the facts reviewed by the court parallel the facts of the present application, applicants believe these slides are not prior art against the invention as claimed in the present application.

This Supplemental Information Disclosure Statement and Form PTO-1449 are

submitted in accordance with 37 C.F.R. § 1.97(b), before the mailing of a first Office Action. Therefore, no fee is believed due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

Respectfully submitted,

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Cathy A. Schetzina

FORM PTO-1449 U.S. Department of Commerce Patent and Trademark Office LIST OF DOCUMENTS CITED BY APPLICANT (Use several sheets if necessary)	Attorney Docket Number 9233-63	Serial No. 09/873,797
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FOREIGN PATENT DOCUMENTS

		Document Number	Date	Country	Class	Subclass	Translation Yes | No
	1.	GB 1 492 997	11/23/77	Great Britain			
	2.	EP 0 031 567	07/08/81	EPO			
	3.	JP 1 254 699	10/11/89	Japan			
	4.	0511903	04/23/92	EP			
	5.	0483465B1	05/06/92	EPO			
	6.	WO93/01802	02/04/93	PCT			
	7.	WO95/09831	04/13/95	PCT			
	8.	EP 0 483 465	08/02/95	EP			
	9.	WO95/30641	11/16/95	PCT			
	10.	EP 0 597 007	10/16/96	EP			
	11.	EP 0 621 777	11/09/96	EP			
	12.	EP0797615B1	01/10/97	EPO			
	13.	WO98/07745	02/26/98	PCT			
	14.	WO99/32134	07/01/99	PCT			
	15.	WO99/65941	12/23/99	PCT			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	16.	Abuchowski, A. and F. F. Davis "Soluble Polymer-Enzyme Adducts" pp. 367-383, *Enzymes as Drugs*, Ed. S. Holcenberg, John Wiley (1981)
	17.	Agarwal et al. "Polymethyacrylate-based Microparticulates of Insulin for Oral Delivery: Preparation and In Vitro Dissolution Stability in the Presence of Enzyme Inhibitors" *International Journal of Pharmaceutics* 225:31-39 (2001)
	18.	Akiyama et al. "The Synthesis of New Derivatives of 1-ß-D-Arabinofuranosylcytosine" *Chem. Pharm. Bull.* 26(3):981-984 (1978)
	19.	Allaudeen et al. "Orally Active Insulin: A Single Insulin Conjugate Selected for Future Studies" 60th Annual Meeting of the American Diabetes Assoc., Atlanta, GA, June 2000 (Abstract)
	20.	Anderson et al. "HIM2, a Novel Modified Insulin, has Improved Systemic Pharmacokinetics in Normal Dogs, Compared to Unmodified Insulin" American Diabetes Association 62nd Annual Meeting, June 2002 (Abstract)

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*EXAMINER Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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	21.	Ansell et al. "Application of Oligo-(14-amino-3,6,9,12-tetraoxatetradecanoic acid) Lipid Conjugates as Steric Barrier Molecules in Liposomal Formulations" *Bioconjugate Chem.* 10:653-666 (1999)
	22.	Aoshima et al. "N^4-Behenoyl-1- ß-D-Arabinofuranosylcytosine as a Potential New Antitumor Agent" *Cancer Research* 37:2481-2486 (1977)
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	24.	Banting et al. "Pancreatic Extracts in the Treatment of Diabetes Mellitus: Preliminary Report" *Can. Med. Assoc. J.* 145(10):1281-1286 (1991)
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	26.	Baudys et al. "Synthesis and Characterization of Different Glycosylated Derivatives of Insulin" *Proceed. Intern. Symp. Cont. Rel. Bioactive. Mater.* 19:210-211 (1992)
	27.	Block, Lawrence H. "Pharmaceutical Emulsions and Microemulsions" *Pharmaceutical Dosage Forms: Disperse Systems* Vol. 2, Ed. Lieberman et al., pp.47-109 (1996)
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	29.	Bone et al. "Successful Treatment of an Insulin Dependent Rat Model of Human Type I Diabetes with Orall Active Insulin" Program and Abstracts, 4th International Workshop on Lessons from Animal Diabetes, Omiya, Japan, November 1994 (Abstract)
	30.	Bone et al. "Successful Treatment of Type 1 Diabetes with Orally-Active Insulin: Studies in The Insulin Dependent BB/S Rat" Program and Abstracts, 55th Annual Meeting of the American Diabetes Association, Atlanta Georgia, June 1995 (Abstract)
	31.	Brange and Volund "Insulin Analogs with Improved Pharmacokinetic Profiles" *Advanced Drug Delivery Reviews* 35:307-335 (1999)
	32.	Brange et al. "Chemical Stability of Insulin. 1. Hydrolytic Degradation During Storage of Pharmaceutical Preparations" *Pharm. Res.* 9(6):715-726 (1992)
	33.	Brange et al. "Chemical Stability of Insulin. 2. Formation of Higher Molecular Weight Transformation Products During Storage of Pharmaceutical Preparations" *Pharm. Res.* 9(6):727-734 (1992)
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	37.	Clement et al. "Effects of Multiple Doses of Orally Administered Hexyl Insulin M2 (HIM2) on Postprandial Blood Glucose (PPG) Concentrations in Type 1 Diabetic (T1) Patients" American Diabetes Association 62nd Annual Meeting, June 2002 (Poster)
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	39.	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Abstract)

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	40.	Clement, Stephen "A Dose-Escalation Study of the Effects of Two Sequential Doses of Oral Modified Insulin on Blood Glucose Concentrations in Patients with Type 1 Diabetes Mellitus" American Diabetes Association Annual Meeting (June 25, 2001) (Poster)
	41.	Conradi et al. "The Influence of Peptide Structure on Transport Across Caco-2 Cells" *Pharm. Res.* 8(12):1453-1459 (1991)
	42.	Coombes et al. "Biodegradable Polymeric Microparticles for Drug Delivery and Vaccine Formulation: the Surface Attachment of Hydrophilic Species Using the Concept of Poly(Ethylene Glycol) Anchoring Segments" *Biomaterials* 18:1153-1161 (1997)
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	47.	Ekwuribe et al. *Mixtures of Drug-Oligomer Conjugates Comprising Polyalkylene Glycol, Uses Thereof, and Methods of Making Same*, U.S. Serial No. 09/873,797, filed 06/04/2001
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	58.	Igarashi et al. "Biologically Active Peptides Conjugated with Lecithin for DDS" *Proceed. Intern. Symp. Cont. Rel. Bioactiv. Mater.* 17:367-368 (1990)
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	61.	King et al. "Preparation of Protein Conjugates with Alkoxypolyethylene Glycols" *Int. J. Peptide Protein Res.* 16:147-155 (1980)
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	76.	Radhakrishnan et al. "Chemical Modification of Insulin with Amphiphilic Polymers Improves Intestinal Delivery," *Proceed. Intl. Symp. Control. Rel. Bioact. Mater.* 25:124-125 (1998) (Abstract)
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	86.	Santiago et al. "Oral Immunization of Rats with Influenza Virus M Protein (M1) Microspheres" *Proceed. Intern.Symp. Cont. Rel. Bioactive. Mater.* 19:116-117 (1992)
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	89.	Soltero et al. *Insulin Polypeptide-Oligomer Conjugates, Proinsulin Polypeptide-Oligomer Conjugates and Methods of Synthesizing Same* U.S. Serial No. 10/382,022, filed 03/05/2003
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	91.	Soltero et al. *Pharmaceutical Compositions of Insulin Drug-Oligomer Conjugates and Methods of Treating Diseases Therewith* U.S. Serial No. 10/382,155, filed 03/05/2003
	92.	Still and McAllister "Effects of Orally Active Modified Insulin in Type 1 Diabetic Patients" *Clinical Pharmacol. Therap.* 69(2):P95 (Feb. 2001) (Abstract)
	93.	Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Slide Presentation Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001
	94.	Still and McAllister "Effects of Orally Active Modified Insulin in Type I Diabetic Patients" Annual Meeting of the American Society for Clinical Pharmacology & Therapeutics, Orlando, FL, March 9, 2001 (Handout)
	95.	Still et al. "Magnitude and Variability of Pharmacokinetic and Glucodynamic Responses to Modified Human Insulin Administered Orally to Healthy Volunteers" *Diabetes Research and Clinical Practice* 56:S77 (2002)
	96.	Still et al. *Methods of Reducing Hypoglycemic Episodes in the Treatment of Diabetes Mellitus*, U.S. Serial No. 10/461,199, filed 06/13/2003

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	97.	Still, J. Gordon "Development of Oral Insulin: Progress and Current Status" *Diabetes/Metabolism Research and Reviews* 18(1):S29-S37 (2002)
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